

# **SPL Process Meeting Meeting Minutes April 10, 2013**

Chair of today's meeting: Pat Cowall-Hanover

Teleconference information:

USA Toll-Free 866-213-2145

USA Paid/International: 609-454-9913

Access code: 273 8216

Teleconference information: How to mute/unmute

#6: Mute

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Agenda and meeting notes:

1. Name of our SPL er/dl process subteam is changing to: SPL Process Subteam

Discussion:

Our SPL group is now the combined SPL ER/DL and SPL Process Subteams. We initially decided to combine names to SPL ER/DL Process subteam. However, we have received feedback that our team discusses more that er/dl topics, and suggested that a new group be formed to discuss these other topics. Instead of creating another subteam, the SPL leaders decided that we should just change our name to SPL Process subteam.

Nothing else has changed: same leaders, same time, same types of discussions,

2. Bulk product listings (Richard Unger)

Is it acceptable / allowable for a bulk product SPL to have the manufacturers labeler code within the metadata of the SPL, while the image of the labeling to be included in the SPL contains the labeler code of the party to which the bulk product is being sold, in this case a third party distributor?

Discussion:

Ruth (Teva):

- Marketing category: drug for further processing.
- Image: image on the bulk container drum -- includes product info, Mfg NDC, Item number of the company receiving the product (ie needed so that they know how to use the product), storage conditions, etc.
- DPL section –use the manufacturers NDC codes

3. Has anyone had any experience with other companies downloading your SPL files from DailyMed and then using it to submit their own labeling information (SPL)? (Tricia Pasek-Perrigo)

Discussion: Issue: has another supplier used the a company's SPL, because it was a similar product, including the NDC number.

- Howard: One client had another company use one of the products as part of a kit. The kit manufacturer used the same drug facts, but changed the effective time, but not the Guid. The kit manufacturer had a validation error but had it overridden. The original manufacturer of the single component had to go back and change the GUID to that section, so it was now unique.
- Tricia's issue is that another supplier used their SPL and their NDC code. Two suppliers produce product for a third party. The other supplier uses a different imprint – therefore it can't use the same NDC code. Somehow supplier #2's SPL should not have passed validation. They are currently working with Lonnie on how to resolve this issue.
- Using other SPL is encouraged for generic products – so that the text is identical.
- New company needs to modify the text appropriately to create a new SPL file.
- Tricia will get back to us.

4. If a branded drug has a labeling change, what section in the CFR covers updating the generic? Would the generic drug just be updated to match, and then reported via the annual report, or would a supplement be required? (OTC manufacturer/Marcia Howard)

Postpone to next meeting so that Marcia can summarize. The detail is provided below.

Discussion:

Information regarding when and how Abbreviated New Drug Application (ANDA) sponsors should submit labeling supplements following labeling revisions to their reference listed drugs (RLDs) may be found in the Guidance for Industry "Revising ANDA Labeling Following Revision of the RLD Labeling". The Guidance states that when a New Drug Application (NDA) serves as a reference listed drug (RLD) for an Abbreviated New Drug Application (ANDA), approved changes in the RLD labeling generally necessitate changes in the labeling of one or more ANDAs using the RLD. Under the Federal Food, Drug, and Cosmetic Act [21 U.S.C.] and Agency regulations, an ANDA product must have the same labeling as the RLD. You may review this Guidance online at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072891.pdf>.

Section 505(j)(2)(A)(v) of the Act [21 U.S.C. 355] states that an abbreviated application for a new drug must contain information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug except for changes required because of differences approved under a petition or because the new drug and the listed drug are produced or distributed by different manufacturers. Similar statements are also found in the regulations at 21 CFR 314.94(a)(8)(iv).

21 CFR 314.94(a)(8)(iv) states:

"Comparison of approved and proposed labeling.

A side-by-side comparison of the applicant's proposed labeling including, if applicable, any Medication Guide required under part 208 of this chapter with the approved labeling for the reference listed drug with all differences annotated and explained. Labeling (including the container label, package insert, and, if applicable, Medication Guide) proposed for the drug product must be the same as the labeling approved for the reference listed drug, except for changes required because of differences approved under a petition filed under 314.93 or because the drug product and the reference listed drug are produced or distributed by different manufacturers. Such differences between the applicant's proposed labeling and labeling approved for the reference listed drug may include differences in expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(5)(F) of the act."

You may review 505(j)(2)(A)(v) of the Act online at: <http://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/pdf/USCODE-2010-title21-chap9-subchapV-partA-sec355.pdf> (page 166 - page 9 of the 34 page PDF document) and 21 CFR 314.94 online at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm>.

5. NLM - PillBox Initiative (Jane Pompei)

- Who would submit an authorized generic for NLM imaging for the PillBox initiative, the NDA holder or distributor?
- How do we get access to the Working Group, WIKI?

Discussion:

- Pillbox is still accepting samples.
- Either or both can send samples to NLM.
- If the reference drug manufacturer submits the samples, then it can filter down to the generics.
- Use the federal register notice from May 2011. You will get an answer back from Terry Yoo.
- This information is on the Pillbox page of the wiki.

WIKI is <http://spl-work-group.wikispaces.com/>

6. Billable unit indexing files: Please help us understand what these are and what we need to do with them (Kathi Lins)

Announcement from SPL in mid February:

The first billing unit indexing SPL files were posted on DailyMed yesterday, Wednesday, February 6, 2013.

Billing unit indexing SPL files are generated by FDA utilizing data provided by members of the National Council of Prescription Drug Programs (NCPDP.) A short overview of NCPDP's billing unit standard is accessible via this hyperlink: [http://www.ncdpd.org/PDF/BUS\\_overview.pdf](http://www.ncdpd.org/PDF/BUS_overview.pdf).

Included in each billing unit indexing SPL file is one unique NDC package code as well the appropriate billing unit (eaches, grams, or milliliters) which describes the quantity of the drug product associated with the NDC identified in the billing unit indexing SPL document.

Since the three-segment NDC is included in both the product's SPL file (the SPL document generated and submitted by drug companies) and the billing unit indexing SPL file, the data in the two aforementioned files can be automatically linked (using the NDC) once imported into a database.

The first batch totaling over 40,000 billing unit indexing SPL files are posted on DailyMed. When new or updated billing unit indexing SPL files are available, they will be transmitted within one business day to NLM for posting on DailyMed.

Here is the hyperlink to the DailyMed web page with the downloadable package of billing unit indexing SPL documents: <http://dailymed.nlm.nih.gov/dailymed/downloadIndexing.cfm>.

Explanation from the SPL Fact Sheet, posted on the SPL Resources page:

The National Council for Prescription Drug Programs (NCPDP) developed the Billing Unit Standard to assist in consistent and accurate billing of pharmaceutical products. Information on the NCPDP Billing Unit Standard may be found at [http://www.ncdp.org/standards\\_quic.aspx](http://www.ncdp.org/standards_quic.aspx). The Billing Unit Index file contains the National Drug Code (NDC) and the corresponding NCPDP Billing Unit (GM, ML or EA). A Billing Unit Index file is created when a Billing Unit designated by NCPDP for a specific NDC is available for a packaged product included in a product SPL file submitted by the drug company.<sup>3</sup>

Billing Unit Indexing files can be downloaded by the public from the National Library of Medicine's DailyMed website.

One file extracted by Terry Brunone:

It contains an NDC code, and what the billing unit is. In this case, EA (for Each)....

```
<subject>
  <manufacturedProduct>
    <manufacturedProduct>
      <asContent>
        <containerPackagedProduct>
          <code code="49999-949-30" codeSystem="2.16.840.1.113883.6.69"/>
        </containerPackagedProduct>
        <subjectOf>
          <characteristic>
            <code code="NCPDPBILLINGUNIT"
codeSystem="2.16.840.1.113883.1.11.19255"/>
            <value code="EA" codeSystem="2.16.840.1.113883.2.13"
xsi:type="CE"/>
          </characteristic>
        </subjectOf>
      </asContent>
    </manufacturedProduct>
  </manufacturedProduct>
</subject>
```

...

Discussion:

- Short answer is that we don't have to do anything. These are used by billers/reimbursements.
- If there is an NDC code...there is a billing unit.
- But billing units don't have to be NDC codes....eg tablets.

7. Related document element: Ranjith Abraham  
What is the “related document element” and how it should be used?

**Discussion:**

Submitted an SPL in 2007. In 2011, this was overridden by another SPL with a different set ID. Every time they try to submit, they get an error message saying to resubmit with a related document ID. What is this?

Howard: This coding allows you to reference/delete an unneeded version of the SPL.

Situation: There are 2 versions of the SPL for the same product. You want to get rid of the old version, presumably incorporating it into the new SPL.

GSK: They had 3 SPLs for related products. FDA told them to combine into 1 SPL. This element allows you to get rid of the 2 unneeded SPLs

- This works well in FDA
- Does not work well for Daily Med.
- As soon as you submit the related document elements, then contact SPL to alert them and ask them to tell Daily Med that they need to get rid of the old SPL.

Related document code is its own element that goes right after the close of the author section.

Data includes: Root id, Set id, and Version number

Documentation from Terry Brunone:

The FDA has been asked to make the process of archiving SPL R3 or duplicate SPL R4 documents on DailyMed easier while still transmitting files from industry to DailyMed without alteration.

FDA proposes the use of a not-yet-utilized SPL data element (the "relatedDocument" data element) to reference the replacement SPL R3 or R4 file. If there is agreement by the SPL community, this data element can then be included in an SPL file transmitted for the purpose of notifying FDA's and NLM's system that an instance of an SPL R3 or duplicate SPL R4 document should be transferred to the DailyMed archives.

Here is an example of the relatedDocument coding:

```
<relatedDocument typeCode="RPLC">
<relatedDocument>
<id root="464239de-45c7-4d2f-a89a-45d303f428bd"/>
<setId root="9ea75e1e-84ef-4605-89ff-dd08a4c94f40"/>
<versionNumber value="3"/>
</relatedDocument>
</relatedDocument>
```

Note: The setId for the SPL R3 or R4 file which needs to be archived (replaced) will be the reference ID.

For an example of the code on DailyMed – search TIMENTIN, open the record, then Download > Download this Label

8. DER registrations – when do manufacturers have to register (Marlene McCallum)
- I'm still confused on when we are required to re-register annually, and when to re-register if "no change"?
  - Is there still the alphabet by first letter of company name? Or did it all change to October-December of each year?
  - CFR 207.21 is still saying by first letter of company name, so I would register for my company in June. Is that correct?

Discussion:

Refer to the following FDA web pages for information

<http://www.fda.gov/Drugs/InformationOnDrugs/ucm135778.htm>

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/DrugRegistrationandListing/UCM322177.pdf>

- As of Oct 2012, you must submit your annual DERs for the following year between Oct – Dec of the current year.
- If you submit any other time of the year, DRLS assumes you are making a correction to your current year's registration.
- If you haven't registered by January 1<sup>st</sup> of the current year, you are out of compliance.
- DECERS site shows the current calendar year.
- Note: FDA is imminently updating the 207 regs – timing doesn't work.
- Device registration process has also adopted this timeline for registering its establishment.
- **Dragan: People are asking if we really have an active subteam for devices.**

9. Effective Date to include in the SPL file: Do the revisions made to the PLR Guidance pertain to SPL? If so, we cannot leave any fields blank. Was there discussion on how to get around this? We only file OTC Drugs (homeopathics). (Samantha Hanigan)

Discussion:

- a. See the minutes from the last meeting.
- b. Recommendation was to put a date that is very far in the future – so that the SPL would never get approved before the date.

10. OTC Monographs: How about a combination product? I have a skin protectant/sunscreen. Until now I just picked one of the monographs, but I think only one is permitted and no matter which I pick all of the active ingredients will not be included. Does anyone have an approach? Carl Strotz

Discussion: Notes from a previous SPL Process team meeting

- As these files are being used, people wanted to make sure that only allowed active ingredients are included as active ingredients in the DLDE SPL file
- The validation procedures will :

- verify that at least one of the active ingredients is in the DLDE Section matches an appropriate monograph product in the list.
- verify that only the allowed monograph active ingredients are in the DLDE section are designated as active ingredients.
- check to make sure that no others are listed
- Goal: make sure manufacturers aren't including ingredients that are not published in a monograph.
- If a product is associated with more than 1 monograph, can you include more than 1 monograph?
  - No, you can only select 1 monograph citation per product.
- SPL resource page will be updated to make sure that the list of valid Monographs is available to everyone to review/check before it is implemented.
- When will this be implemented?
  - Not yet, but maybe soon
  - Lonnie is waiting for the list to be perfect before implementing.
- Suggestion: Need to make sure that we can translate this into people-speak
  - Look at the SPL resource page
  - They need to check their monographs to be consistent with the list

11. Drug listing process: Please explain the drug listing process – ie which establishments should be listed in the drug listing section for SPL. (Angie Giella)

Discussion:

FDA has training on this:

[http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm155705.htm#spl\\_training\\_mat](http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/ucm155705.htm#spl_training_mat)

Include active sites (not inactive) involved in the manufacturing of the product:

- API manufacturers
- Drug product manufacturing
- Testing sites: API and drug product
- Packaging
- Labeling
- Sterilization.

You do not need to include:

- Sites involved in API before the final API site
- Suppliers of inactive ingredients
- Suppliers of device components and packaging (eg vials, cartridges, pen components, needles, etc)

12. Dun and Bradstreet –have they come back with anything. Dale Ianetti (Merck)

Discussion:

- D&B haven't come back with anything about the pilot.
- One company had a merger and had a lot of issues

- US sites are relatively easy to update by working with D&B US.
- Biggest problem is with foreign sites – because they need to work with the foreign branches of their D&B branches. Work with the US foreign
- How did you get names of someone at D&B. Usually the larger companies have dedicated representatives.
- Dale volunteered to pass on her D&B contact information. Dale.lannetti@merck.com

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Long-term topics that we want to keep on our radar screen:

- Registering of excipients under FDASIA:
  - When will we be seeing more info on this?
  - Are OTCs required to register excipient manufacturers under FDASIA?
- Migration of ER/DL data to IDMP – this discussion should go to the SPL tech team, with a follow-up to our SPL Process Team